

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US04/21487

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(7) : A61K 38/00, 38/36; C07K 4/12, 14/745 US CL : 530/300, 345 According to International Patent Classification (IPC) or to both national classification and IPC																			
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 530/300, 345																			
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched																			
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) US-PATS, US-PGPUBS, CAPLUS, BIOSIS, MEDLINE, WPIDS																			
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 10%;">Category *</th> <th style="width: 80%;">Citation of document, with indication, where appropriate, of the relevant passages</th> <th style="width: 10%;">Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>HORTIN, G.L. Sulfation of Tyrosine Residues in Coagulation Factor V. <i>Blood</i>, 1 September 1990, Vol 76, No 5, pages 946-952, especially page 950.</td> <td>1, 6-8, 10, 43-49, 51</td> </tr> <tr> <td>X, P</td> <td>BECK, D.O., et al. The contribution of amino acid region ASP695-TYR698 of factor V to procofactor activation and factor Va function. <i>Journal of Biological Chemistry</i>, 23 January 2004, Vol 279, No 4, pages 3084-3095.</td> <td>1-8, 10, 43-49, 51</td> </tr> <tr> <td>A</td> <td>PITTMAN, D.D., et al. Posttranslational sulfation of factor V is required for efficient thrombin cleavage and activation and for full procoagulant activity. <i>Biochemistry</i>, 7 June 1994, Vol 33, No 22, pages 6952-6959, especially page 6956.</td> <td>1-8, 10, 43-49, 51</td> </tr> <tr> <td>A</td> <td>HORTIN, G.L., et al. Allosteric changes in thrombin's activity produced by peptides corresponding to segments of natural inhibitors and substrates. <i>Journal of Biological Chemistry</i>, 15 April 1991, Vol 266, No 11, pages 6866-6871, especially pages 6866 and 6867.</td> <td>1-8, 10, 43-49, 51</td> </tr> <tr> <td>A</td> <td>PREVIERO, A., et al. Specific sulfonation of tyrosine, tryptophan, and hydroxy-amino acids in peptides. <i>Biochimica et Biophysica Acta</i>, 14 December 1979, Vol 581, No 2, pages 276-282, especially page 276.</td> <td>1-8, 10, 43-49, 51</td> </tr> </tbody> </table>		Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	HORTIN, G.L. Sulfation of Tyrosine Residues in Coagulation Factor V. <i>Blood</i> , 1 September 1990, Vol 76, No 5, pages 946-952, especially page 950.	1, 6-8, 10, 43-49, 51	X, P	BECK, D.O., et al. The contribution of amino acid region ASP695-TYR698 of factor V to procofactor activation and factor Va function. <i>Journal of Biological Chemistry</i> , 23 January 2004, Vol 279, No 4, pages 3084-3095.	1-8, 10, 43-49, 51	A	PITTMAN, D.D., et al. Posttranslational sulfation of factor V is required for efficient thrombin cleavage and activation and for full procoagulant activity. <i>Biochemistry</i> , 7 June 1994, Vol 33, No 22, pages 6952-6959, especially page 6956.	1-8, 10, 43-49, 51	A	HORTIN, G.L., et al. Allosteric changes in thrombin's activity produced by peptides corresponding to segments of natural inhibitors and substrates. <i>Journal of Biological Chemistry</i> , 15 April 1991, Vol 266, No 11, pages 6866-6871, especially pages 6866 and 6867.	1-8, 10, 43-49, 51	A	PREVIERO, A., et al. Specific sulfonation of tyrosine, tryptophan, and hydroxy-amino acids in peptides. <i>Biochimica et Biophysica Acta</i> , 14 December 1979, Vol 581, No 2, pages 276-282, especially page 276.	1-8, 10, 43-49, 51
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<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.																			
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed																			
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family																			
Date of the actual completion of the international search 17 March 2005 (17.03.2005)																			
Date of mailing of the international search report 18 JUL 2005																			
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230																			
Authorized officer Lora E Barnhart Telephone No. 571-272-1600																			
CONNORA E. SAUCER PRIMARY EXAMINER																			

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**Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)**

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material

- a sequence listing  
 table(s) related to the sequence listing

b. format of material

- in written format  
 in computer readable form

c. time of filing/furnishing

- contained in the international application as filed  
 filed together with the international application in computer readable form  
 furnished subsequently to this Authority for the purposes of search

2.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-8, 10, 43-49 and 51

Remark on Protest

  

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

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**BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**  
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-8, 10, 43-49, and 51, drawn to a peptide with a sequence comprising SEQ ID NO. 10 and compositions comprising said peptide.

Group II, claim(s) 9, 50, 82-86, and 92-101, drawn to methods of treatment comprising administering the product of Group I.

Group III, claim(s) 11-18, 20, 52-58, and 60, drawn to a peptide with a sequence comprising SEQ ID NO. 11 and compositions comprising said peptide.

Group IV, claim(s) 19, 59, 87-91, and 102-111, drawn to methods of treatment comprising administering the product of Group III.

Group V, claim(s) 21-24, 26, 61-64, and 66, drawn to a peptide with a sequence comprising SEQ ID NO.s 12, 13 and compositions comprising said peptide.

Group VI, claim(s) 25 and 65, drawn to methods of treatment comprising administering the product of Group V.

Group VII, claim(s) 27-29, 31, and 67-69, drawn to a peptide with a sequence comprising SEQ ID NO. 14 and compositions comprising said peptide.

Group VIII, claim(s) 30 and 70, drawn to methods of treatment comprising administering the product of Group VII.

Group IX, claim(s) 32-35, 37 71-74, and 76, drawn to a peptide with a sequence comprising SEQ ID NO.s 7, 8 and compositions comprising said peptide.

Group X, claim(s) 36 and 75, drawn to methods of treatment comprising administering the product of Group IX.

Group XI, claim(s) 38-40, 42, 77-79, and 81, drawn to a peptide with a sequence comprising SEQ ID NO. 9 and compositions comprising said peptide.

Group XII, claim(s) 41 and 80, drawn to methods of treatment comprising administering the product of Group XI.

The inventions listed as Groups I-XII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: they are not unified by a special technical feature. PCT Rule 13.2 defines a "special technical feature" as a technical feature that defines a contribution that each claimed invention, considered as a whole, makes over the prior art.

The claims are drawn to six peptides and methods for using them. The product claims are broadly drawn to peptides comprising specific 4- and 5-amino acid sequences, said sequences being found in the human blood clotting factor Va. The use of the open-language term "having" includes all peptides comprising these sequences, regardless of their overall length. The product claims therefore read on Factor Form PCT/ISA/210 (extra sheet) (January 2004)

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Va itself, the sequence of which is well known in the art (Jenny et al., 1987, Proc. Natl. Acad. Sci. USA 84: 4846-4850) and cannot be considered a special technical feature.

Because unity of invention is lacking, the product Groups can be separated from the method Groups.